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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/494,282	01/18/2000	Sergey A. Selifonov	02-028930US	3228

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EXAMINER

ZHOU, SHUBO

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 11/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/494,282	Applicant(s) SELIFONOV ET AL.	
	Examiner Shubo "Joe" Zhou	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 99-112 is/are pending in the application.
- 4a) Of the above claim(s) 102-104 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 99-101, 105-112 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>filed 10/6/03</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' amendment and request for reconsideration in the communication filed on 8/4/03 is acknowledged and the amendments entered.

This application contains claims 102-104 drawn to an invention nonelected. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections-35 USC § 112

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 99-101, 105-112 are rejected under 35 U.S.C. 112 , second paragraph, as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase “two or more parental character strings representing one or more polynucleotides or polypeptides” in claims 99, 105 and 112, and their respective dependent claims is confusing and indefinite. It is unclear how two or more parental character strings represent one or more polynucleotides or polypeptides. It is noted that the claim is amended to recite “two or more parental character strings”. Does applicant mean to recite “two or more parental character strings representing two or more polynucleotides or polypeptides”?

The phrase “the one or more parental character strings” in step c) of claims 99, 105 and 112, and their respective dependent claims lacks clear antecedent basis. “Two or more parental

character strings” is recited in step a) and it is unclear what is “the one or more parental character strings” in step c).

Furthermore, claim 112 comprises steps a), c) and d). Clearly, step b) is missing and it is unclear what it constitutes.

Claim Rejections-35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 99-101, and newly added claims 105-112 are rejected under 35 U.S.C. 103(a) as being unpatentable over Venkatasubramanian et al. (IDS document: J. Chem. Inf. Comput. Sci. Vol. 35, pages 188-195, 1995) in view of Dahiyat et al. (IDS document: US Patent No. 6,403,312).

Claims 99-101, and newly added claims 105-112 are drawn to a computational method of identifying a set of oligonucleotides for use in an in vitro recombination procedure.

Venkatasubramanian et al. discloses a computational method of designing new chemical polymers using genetic algorithm. The method comprises providing two mating parents of chemical polymer and manipulating the mating parents using such genetic operators as crossover and mutation to produce derivative chemical polymers with desired properties. See page 188, right column, bottom paragraph and page 189, left column. The genetic operators also comprise insertion and deletion. See page 190, left column.

While Venkatasubramanian et al. does not explicitly indicate designing proteins or nucleic acids using the genetic operators, it would have been obvious that an ordinary skill in the art would have been motivated to modify Venkatasubramanian et al. for other polymers such as proteins and nucleic acids because the latter are two major types of chemical polymers and have been studied for centuries by recombination and other mutational methods. There would have been a plethora of prior art references teaching of making novel proteins or nucleic acids by recombination or mutation. For example, Dahiyat et al. disclose a method of protein design automatic for protein libraries. As an example, Dahiyat et al. teach of a procedure for making and computationally screening an array of mutant polypeptides of β -lactamase TEM-1. See columns 30-34. The procedure comprises providing data for the sequence of TEM-1 and computationally identifying positions of the sequence that are to be allowed to change their identities (column 30). The procedure also comprises computationally prescreening on TEM-1 by using Dead End Elimination optimization method to find the lowest energy, ground state sequences (column 31). The multiple peptide sequences are generated by taking consideration of the stability of the conformation of the polypeptide and the stability of the conformation of the enzyme's active site. Also see column 7. To synthesize the recombinant peptide sequences, a set of overlapping oligonucleotides including all desired mutations are identified and synthesized to

be used to generate a mutant sequence library. See column 32. The method also comprises additional genetic operations such as PCR multiplication using the identified oligonucleotides, which would introduce mutations at the various positions selected.

While neither Venkatasubramanian et al. nor Dahiyat explicitly teaches of identifying frameshift mutations and removing the mutant derivatives as required in the claims, Venkatasubramanian et al. does indeed disclose ways to let highly fit individuals reproduce more and “the least fit individuals would be less likely to get selected for reproduction and thus die eventually”. See page 189, left column. Since Venkatasubramanian et al. teaches of using insertion or deletion as genetic operators, it would have been obvious to an ordinary skill in the art that such operators would inevitably produce frameshift mutations, some of which would be less fit and would die out, thus being removed, eventually in the computational procedure.

This rejection is reiterated from the previous Office action and maintained for reasons of record.

Applicants argument detailed on pages 7-8 of the communication filed 8/4/03 is essentially on the ground that the Venkatasubramanian reference does not teach selecting a crossover point by “pairwise homology”. However, such limitation is not required in the claims. Further, applicants argue that the Venkatasubramanian reference deals with industrial polymer not polynucleotides or polypeptides. This is not persuasive because Venkatasubramanian reference does discuss recombination of nucleic acids (see page 189, left column), and Dahiyat et al. clearly teaches polynucleotides and polypeptides. Applicants further argue that Dahiyat et al. does not teach selecting a crossover point by “pairwise homology”. As set forth above, this is not a limitation required in the claims.

Claim Objections, Warning

Applicant is advised that should claims 99-101 be found allowable, claims 105-107 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, respectively. Also, claim 112 is a duplicate of claims 99 and 105. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL.

Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and

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1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to:

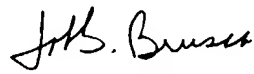
Shubo "Joe" Zhou, Ph.D., whose telephone number is (703) 605-1158. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst Tina Plunkett whose telephone number is 703)-305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

S. "Joe" Zhou, Ph.D.



Patent Examiner



JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER